Achalasia is a disorder of the esophagus, in which the esophagus has abnormal muscle activity and does not possess the ability to move food into the stomach. The major symptom is usually difficulty with swallowing. Complications may include regurgitation, gastroesophageal reflux, pulmonary aspiration, and perforation of the esophagus. Achalasia affects approximately 1 in every 100,000 people in the United States.

The etiology of achalasia remains largely unknown; however, the occurrence of familial achalasia and its association with defined genetic syndromes have indicated that in some cases achalasia can be caused by genetic anomalies. EGL tests for genes known to cause the following achalasia-associated syndromes:

- Triple A syndrome (Achalasia-Addisonianism-Alacrima) or Allgrove syndrome
- Moyamoya diesase-6 with achalasia
- Alacrima, achalasia, and mental retardation syndrome
- Baraister-Winter Cerebrofrontofacial syndrome
- Autoimmune Polyendocrine syndrome type with or without Reversible Metaphyseal dysplasia
- Ataxia, posterior column, with retinitis pigmentosa (PCARP)

References:

3. OMIM.

Genes

AAAS, ACTB, AIRE, FLVCR1, GMPPA, GUCY1A1

Indications

The test is indicated for:

- Individuals with a clinical diagnosis of achalasia.

Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.
Specimen Requirements

Submit both of the following specimens

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen<sup>TM</sup> Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.